Amendment #1 to RFP-NIH-NIAID-DAIDS-04-04
"Microbicide Design and Development Teams"

This amendment provides questions submitted by potential applicants/offerors and the responses provided by NIAID. The responses are offered for information only and do not modify or become part of this solicitation. This Amendment will be updated as needed to add further questions and their related responses. All potential offerors are advised to refer back to this Amendment #1 for additional Questions & Answers.

Amendment to Solicitation No.:	NIH-NIAID-DAIDS-04-04
Amendment No.:	One (1) 1st Posting: Questions 1 – 11 (posted June 4, 2004) 2nd Posting: Question 12 (posted July 7, 2004)
Issue Date:	July 7, 2004
Effective Date:	July 7, 2004
Proposal Due Date:	August 13, 2004,at 4:00 P.M. local time
Issued By:	Thomas P. Hastings Contracting Officer NIH/NIAID Contract Management Program 6700 B Rockledge Drive Room 3214, MSC 7612 Bethesda, Maryland 20892-7612
Point of Contact:	Donald E. Collie, Contract Specialist dc128b@nih.gov
Name and Address of Offeror:	To All Potential Offerors

The above numbered solicitation is amended as set forth below. The hour and date specified for receipt of proposals **HAS NOT** been extended. Offerors must acknowledge receipt of this amendment. Failure to receive your acknowledgement of this amendment may result in the rejection of your offer. This amendment shall be acknowledged in the following manner:

- By acknowledging receipt of this amendment on each copy of the offer submitted.

The following answers are provided to frequently asked questions and inquires we have received.

QUESTION 1: Note 5 to Offerors says that collaboration with NIAID-supported prevention trials networks is encouraged, but not required for any human clinical trials proposed. If the Offeror chooses to collaborate with an NIAID-sponsored trial network to perform clinical trials with the proposed microbicide product(s), a "letter-of-intent" from the appropriate network should be submitted with the proposal. Who is the appropriate contact in the HIV Prevention Trials Network (HPTN) for discussion of potential future collaborations?

ANSWER: The appropriate contact for the HPTN is Dr. Ian McGowan, chair of the Microbicide Science Working Group. He can be reached at (310) 206-3580 or via email at imcgowan@mednet.ucla.edu.

QUESTION 2: We note that there has also been a program announcement (PA) entitled Integrated Preclinical/Clinical Program for HIV Topical Microbicides (IPCP-HTM) and are currently trying to determine what the principal differences are between this and the above RFP, and whether one is more appropriate for our purposes. We wondered if you could shed any light on how the aims of this IPCP-HTM differ from those of the MDDT RFP?

ANSWER: The IPCP-HTM is a mechanism for funding a multiproject, multidisciplinary cooperative agreement or program project grant. This is an established program that supports microbicide product development linked with research. These grants usually combine 2 or 3 research projects linked to the central theme of development of a specific microbicide concept or strategy with cores that serve multiple projects. Some of the research projects are very basic in nature e.g., development of new/improved models for evaluating safety or efficacy but these basic projects must be well integrated into the overall plan for advancement of the microbicide candidate being studied such that they contribute to the progress of the candidate through the development paradigm. The IPCP-HTM is designed to support translational research that advances a microbicide concept to initial exploratory clinical studies where refinement and optimization of the candidate can be achieved expeditiously in an iterative manner given the close association of the clinical components with the preclinical and research components of the entire multi-project program. However, it is not expected that all IND-enabling activities will be conducted with the support of an IPCP-HTM award. Further, because the IPCP-HTM seeks to increase the array of approaches and availability of potential candidates suitable for advancement into clinical trials, this Program also supports discovery through early preclinical development where it is not feasible for the proposed microbicide concept to advance to the point of clinical testing within the period of the award. Thus, clinical studies are not a requirement of the IPCP-HTM but an option. With the IPCP-HTM providing a spectrum of funding opportunities for research spanning discovery through preclinical development into pilot clinical studies, support is available to translate basic microbicide discoveries to innovative applied entities.

In contrast, the Teams Program is designed to facilitate more unified and traditional product development efforts that culminate in the initiation of a Phase I clinical trial within the period of award. Additional basic research on developing further optimized iterations of the microbicide candidate can be included but a clear development path for moving the microbicide into clinical trials must be thoroughly developed and clearly articulated. All the necessary technical parts of product development (e.g., GMP process development and manufacture, preclinical toxicology, regulatory compliance) as well as the science supporting the basic microbicide concept and its development and optimization constitute critical, required elements of a successful Teams Contract. The Teams Program is targeted toward the private sector and academic investigators with experience and expertise in focused product development distinct from research that is solely hypothesis-driven. As such, a milestone-based contract mechanism is used to guide the critical path development of a specific microbicide concept where yearly renegotiation of milestones takes place to account for unexpected difficulties and emerging advances. It is intended that the Teams Program will provide an opportunity for sustained, streamlined support for all IND-enabling and GMP activities required for initiating a Phase I study of a promising microbicide candidate within the five year award period.

QUESTION 3: Can DAIDS indicate if there is a preference for, or concern with, any device concepts (e.g., intravaginal ring, etc.) that could be incorporated into a proposal to this program?

ANSWER: The Teams do not support the development of a device in the absence of a microbicide. A device (i.e., other than the applicators currently being used to deliver microbicide candidates in Phase 2/2b/3 trials) may be used to deliver a single or combination microbicide if the device confers a significant advantage over the delivery of a single or combination microbicide in the absence of the device. In the case of microbicides currently being evaluated in clinical trials, the development plan proposed must demonstrate sufficient novelty of the device-associated microbicide concept that distinguishes it from the microbicide or device alone.

QUESTION 4: The scope of any proposal responding to this RFP is a function of the published work scope and the available funding resources. In order to construct an appropriately responsive proposal, information is requested on the anticipated size of each individual award to be made under this RFP; or, the total amount of funds available for the entire program and the expected number of awards. Can this information please be provided?

ANSWER: The contract award process is a competitive process. No information is available regarding funding or the expected number of awards.

QUESTION 5: NIAID offers contract services, independent of this RFP, to support microbicide development. Since access to these services would complement a proposal responding to this RFP, information on what contract services are available, and how they could be accessed for purposes of this RFP would be useful to organizations intending to submit proposals. Can a listing of available support contracts for microbicide development be provided so these resources can be appropriately incorporated into our proposal?

ANSWER: A listing of development resources can be found at: http://www.niaid.nih.gov/daids/pdatguide/overview.htm and http://dtp.nci.nih.gov/docs/dart.html. However, it is intended that a Teams contract will provide support for all development activities required for moving a microbicide candidate into a Phase I study within the period of award. (See ANSWER to Question 2)

QUESTION 6: Is there a preferred therapeutic class for a microbicide candidate or is it the case that DAIDS is equally willing to fund any class of potential microbicide compounds? Are there specific classes of compounds that DAIDS would prefer not to be the subject of a proposal to this program?

ANSWER: Concepts including nonoxynol-9 are not responsive. In addition, the simple mixing and dilution of products currently in clinical trial to create a combination is not responsive e.g. candidate A at dose of 1% + candidate B at dose of 0.5% cannot be mixed to create a combination of candidate A 0.5%:candidate B 0.25% unless a compelling scientific rationale can be provided demonstrating expected superiority of such a product.

QUESTION 7: Can DAIDS provide input regarding how advanced in development a microbicide candidate should be in order to serve as the subject of an appropriately responsive proposal? For example, can DAIDS indicate what type of data should already be available for an appropriate microbicide candidate for this program?

ANSWER: The goal of a Teams Contract is to advance a microbicide candidate into a Phase I trial within the period of the award. This objective is based on a development plan with specific milestones that are feasible and likely to be achieved during the course of the award. Thus, it would be expected that a lead candidate is identified, it's structure described, and enough preliminary data provided that it can be produced. In addition, the lead should be justified with data that it is a relevant microbicide approach e.g., demonstration of in vitro activity as a virucidal agent or that it interferes with infection via another mechanism (2).

QUESTION 8: Is the issue of contraceptive capability for a microbicide candidate for this program relevant?

ANSWER: Contraceptive activity of the proposed microbicide concept is not germane to the Teams Program.

QUESTION 9: Are commitments from consortium members regarding intellectual property issues relevant to proposals acceptable if they are contingent upon receipt of the RFP award?

ANSWER: Yes

QUESTION 10: In note 5 to offerors, a "draft agreement signed by all partners involved..." is referenced. Can DAIDS explain the nature of a signed "draft agreement," relative to a final agreement? Of what relevance is a signed "draft" agreement? This type of agreement is also referenced on page 58.

ANSWER: The intent of a draft agreement is for all parties to be aware of the future relationships and what is involved in working on a project such as this. It demonstrates that all parties/scientists have been consulted with appropriate authorities in their institutions and everyone is aware of the legal environment in which product development takes place. It is still signed by someone with binding authority at all institutions involved and is stamped "Draft."

QUESTION 11: Since full negotiation of intellectual property agreements will involve costs to responding organizations, and there is risk that a responding organization will not actually receive an award, is it acceptable to submit letters that commit to future "good faith" negotiations upon receipt of an award?

ANSWER: Yes, as long as those letters are signed by persons with binding authority from all institutions involved.

QUESTION 12: If the proposal to the HPTN or its equivalent would be instrumental in developing the Phase I protocol in the future, is there a time frame that I can use to put into my Gantt chart for the proposal? We do not want to get to a point where we are ready to write an IND but not have a firm commitment from the clinical component or a plan at least in draft form.

ANSWER: If the Offeror plans to have their Phase I study conducted through the network i.e., HPTN, then a letter of intent (as outlined in Note 6 To Offeror) from the network is needed. A general timeline for development of such a protocol should be obtained from the network.

In contrast, if the Offeror plans to conduct the Phase I trial independent of an existing DAIDS/NIAID clinical network, then a rudimentary, draft protocol should be submitted with the proposal. This would not have to be a finalized protocol, but the basics of the protocol should be delineated, and particular attention should be paid to human subjects protection as detailed in the RFP. The level of detail should provide enough information from which to ascertain the technical expertise of the Offeror and the Offeror's understanding of the crucial elements in such a trial.